Serial No.: 09/835,273 Filed: 4/13/2001 Page: 2 of 13

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the Application.

1. (Currently amended) A method for analysis of proteins in a biological system comprising:

providing a biological system;

sampling the biological system at multiple time intervals to provide multiple samples, each sample containing multiple proteins;

submitting each of the multiple samples to a separation technique to provide multiple protein samples suitable for analysis by mass spectrometry; and

analyzing the multiple samples to determine changes in abundance of proteins as a function of time, said analyzing including

allocating the multiple protein samples for the multiple samples among mass spectrometry systems in a parallel array of mass spectrometry systems, each mass spectrometry system <u>analyzing a different one of the multiple protein samples adapted for protein analysis</u> and providing mass spectral data indicating identity and abundance of one or more proteins,

directing mass spectral data from each of the mass spectrometry systems in said array to a common computing device, and

collating said mass spectral data from each of the mass spectrometry systems as a function of time of sampling of the biological system.

- 2. (Previously presented) The method of claim 1 further comprising displaying said collated data as a function of protein identity, protein abundance, and time.
 - 3. (Canceled)

Docket No.: 12800-003001 (1002US) Applicants: James R. LaDine, et al.

Serial No.: 09/835,273 Filed : 4/13/2001 : 3 of 13

Page

4. (Canceled)

5. (Previously presented) The method of claim 1 wherein said array of mass spectrometry systems includes at least 5 mass spectrometers.

- 6. (Previously presented) The method of claim 1 wherein analyzing the multiple samples includes analyzing the multiple samples to determine changes in abundance of 500 proteins or more.
- 7. (Previously presented) The method of claim 1 wherein analyzing the multiple samples includes analyzing the multiple samples to determine changes in abundance of about 5000 proteins or more.
- 8. (Previously presented) The method of claim 1 wherein the separation technique includes use of one or more separation apparatus and said common computing device communicates with each of said separation apparatus.
- 9. (Previously presented) The method of claim 1 wherein the separation technique includes use of liquid chromatography.
- 10. (Previously presented) The method of claim 8 wherein the separation apparatus includes a magnetic particle separation apparatus.
- 11. (Previously presented) The method of claim 38 wherein the array of separation apparatus treat multiple samples in parallel.
- 12. (Previously presented) The method of claim 1 wherein the separation technique includes treating each of the multiple protein samples with a protease to produce peptides and the mass spectral data includes amino acid sequence data that can be compared to amino acid sequence data derived from a data base.

Serial No. : 09/835,273 Filed : 4/13/2001 Page : 4 of 13

13. (Previously presented) The method of claim 12 wherein said mass spectrometry systems are LC-TMS mass spectrometers.

14. (Previously presented) The method of claim 1 further comprising:

exposing a first instance of the biological system to a stimulus and maintaining a second instance of the biological system free of the stimulus;

wherein sampling, submitting, and analyzing include sampling, submitting, and analyzing each of the first and the second instances; and

correlating mass spectral data includes comparing mass spectral data from the first and the second instances.

15. (Original) The method of claim 14 comprising separately analyzing samples from said first component and second component.

16. (Previously presented) The method of claim 43 wherein the perturbation results from exposure of the biological system to heat, light, cold, motion, agitation, cellular material, or a drug.

- 17. (Previously presented) The method of claim 1 wherein the time interval is about 5 to 60 seconds.
- 18. (Previously presented) The method of claim 1 wherein the time interval is about one minute to one hour.

Claims 19-21. (Cancelled)

22. (Currently amended) A method for analysis of proteins in a biological system comprising:

providing a biological system containing proteins;

Docket No.: 12800-003001 (1002US) Applicants: James R. LaDine, et al.

Serial No.: 09/835,273 Filed : 4/13/2001

Page : 5 of 13

exposing the biological system to a stimulus;

after exposing the biological system to the stimulus, sampling the biological system at multiple time intervals to obtain multiple samples, each sample containing multiple proteins;

treating the multiple samples by a parallel separation technique to provide multiple protein samples suitable for analysis by mass spectrometry;

providing a parallel array of mass spectrometer systems capable of simultaneous analysis of as many protein samples as there are spectrometer systems in said array;

allocating the multiple protein samples among the mass spectrometry systems in the parallel array of mass spectrometry systems such that each mass spectrometry system analyzes a different one of the multiple protein samples to obtain mass spectral data indicating identity and abundance of proteins in said multiple protein samples;

communicating the mass spectral data to a common computing device; and correlating said mass spectral data as a function of time.

- 23. (Previously presented) The method of claim 22 wherein the parallel separation technique is performed using a parallel magnetic particle separation device.
- 24. (Previously presented) The method of claim 23 wherein the parallel array of mass spectrometry systems includes an array of LC-MS spectrometer systems.
- 25. (Previously presented) The method of claim 24 wherein the array includes 6-20 mass spectrometers.
- 26. (Previously presented) The method of claim 25 wherein the time intervals are in the range of 5 seconds to 10 minutes.
- 27. (Previously presented) The method of claim 26 wherein the analysis includes analysis of about 500 proteins or more.

Serial No.: 09/835,273 Filed: 4/13/2001 Page: 6 of 13

28. (Previously presented) The method of claim 23 wherein the central computer communicates with the parallel magnetic particle separation device.

29. (Currently amended) A system for mass spectrometric analysis of proteins in a biological system, the system comprising:

a parallel sample separation apparatus adapted to receive multiple samples of a biological system taken at multiple time intervals, and separate the multiple samples in parallel to obtain multiple protein samples for analysis by mass spectrometry;

a parallel array of mass spectrometry systems adapted to receive the multiple protein samples from the separation apparatus and analyze the multiple protein samples in parallel to generate mass spectral data indicating identity and abundance of proteins, each mass spectrometry system analyzing a different one of the multiple protein samples; and

a computing device communicating with the parallel array of mass spectrometry systems and the parallel separation apparatus, the computing device being adapted to analyze the mass spectral data from the parallel array of mass spectrometry systems and collate the mass spectral data as a function of time of sampling.

4

- 30. (Previously presented) The system of claim 29, wherein the parallel separation device is a parallel magnetic particle separation device.
- 31. (Previously presented) The system of claim 29, wherein the parallel separation device is a parallel chromatography separation device.
- 32. (Previously presented) The system of claim 29, wherein the computing device is adapted to collate the mass spectral data as a function of time.
- 33. (Previously presented) The system of claim 29, further comprising a graphical user interface that can be searched, queried, or filtered to display selected collated data.

Serial No. : 09/835,273 Filed : 4/13/2001 Page : 7 of 13

34. (Previously presented) The system of claim 29 wherein the parallel array of mass spectrometry systems includes at least 5 mass spectrometers.

- 35. (Previously presented) The system of claim 29, wherein the parallel array of mass spectrometry systems includes at least 20 mass spectrometers.
- 36. (Previously presented) The system of claim 29, wherein the parallel array of mass spectrometry systems is adapted to generate mass spectral data including peptide fragment mass spectra, and the computing device is adapted to analyze the mass spectral data in conjunction with an amino acid sequence derived from a database.
- 37. (Previously presented) The system of claim 29, wherein the parallel array of mass spectrometry systems include a liquid chromatograph-tandem mass spectrometer system.
- 38. (Previously presented) The method of claim 8 wherein a first portion of the multiple protein samples are allocated among the mass spectrometry systems before a second portion of the multiple protein samples have been provided by the separation technique.
- 39. (Previously presented) The method of claim 8 wherein the separation technique includes use of an array of parallel separation apparatus.
- 40. (Previously presented) The method of claim 39 wherein the number of separation apparatus in the array of parallel separation apparatus is equal to the number of mass spectrometry systems in the array of parallel mass spectrometry systems.
- 41. (Previously presented) The method of claim 11 wherein the array of mass spectrometry systems treat multiple samples in parallel.

Serial No. : 09/835,273 Filed : 4/13/2001 Page : 8 of 13

42. (Previously presented) The method of claim 41 wherein treatment of multiple samples by the array of separation apparatus is carried out in parallel with treatment of multiple samples by the array of mass spectrometry systems.

- 43. (Previously presented) The method of claim 1 further comprising exposing the biological system to a perturbation, wherein sampling of the biological system occurs at multiple time intervals after the exposure of the biological system to the perturbation.
- 44. (Previously presented) The method of claim 1 further comprising inferring interactions over time between and among proteins in the biological system.
- 45. (Previously presented) The method of claim 2 wherein protein abundance is expressed as relative abundance of proteins in each of the multiple samples.